REMARKS

Claims 1, 2, 4-11 and 15 are in this application. Claim 17 was cancelled in the previous response.

According to the Official Action, claims 1, 2, 4-11 and 15 are rejected as being obvious in view of Skinhoj (WO 99/12524). This rejection is respectfully traversed.

The examiner has cited WO 99/12524 (Nycomed) [(Modified Release Multiple-Units Compositions of Non-Steroid Anti-inflammatory drug substances (NSAIDs)] against all the claims pending in this application, namely claims 1, 2, 4-11, and 15 on obviousness grounds.

The abstract and claim 1 in the PCT publication WO 99/12524 relates to "An oral pharmaceutical modified release multiple-units composition in unit dosage form for administration of a therapeutically and/or prophylactically effective amount of a non-steroid anti-inflammatory drug substance (an NSAID substance), comprising two fractions wherein the first fraction of multiple units aids in quick release of the NSAID substance and the second fraction of multiple units aids in extended release of the NSAID substance. A broad category of NSAIDs has been disclosed in the cited reference, but only lornoxicam containing compositions have been provided in the examples. Nowhere in the citation is there disclosure, teaching or motivation to make unit dosage tablet compositions comprising nimesulide wherein nimesulide is present both in the fast release layer and in the extended release layer.

The invention claimed in this application does not relate to a multiple unit dosage form; instead it specifically relates to a compressed unit dosage form (tablet) comprising particles of nimesulide wherein nimesulide is present in both the fast as

well as extended release layer. It is not obvious from the disclosure of WO99/12524 to one having ordinary skill in art to formulate single unit tablet compositions comprising nimesulide as simple particles in admixture with other excipients; wherein nimesulide is present in both the fast as well as extended release layer.

Nowhere in the citation is there disclosure, teaching or suggestions describing compressing the multiple units to a tablet dosage form. The multiple units cannot be formulated into a tablet dosage form since the application of compression force in a tablet compression machine will lead to rupturing of the coated multiple units resulting in loss of uniformity of the coating layer over the entire unit (pellet or granule) thus producing variable and unpredictable release of the active agent from such compressed forms, if at all it is made into such form. The invention claimed in this application involves the simple treatment of nimesulide with the excipients and then compressing them into tablets. The claimed product is easy to formulate and does not involve the cumbersome step of producing pellets and further coating them to obtain units for producing sustained release of the drug. The claimed invention invention is specifically a layered tablet composition wherein one layer i.e. the extended release layer comprises a release controlling polymer and the other layer is a fast release layer wherein nimesulide is present in both the fast as well as extended release layer.

Moreover, the compositions disclosed in the above cited reference relate specifically to lornoxicam (Refer to page 27, lines 4-7 page 53, lines 11-12 and examples 1-18, pages 53-83 of the cited reference). It is not taught in the citation to select from a large class of NSAIDs, a specific drug i.e. nimesulide whichcan be made into a ready-to-use single unit tablet dosage form that can be administered to the patient directly. The citation discloses only multiple units, which need to be first formulated into a suitable dosage form prior to administration to a patient. Nowhere, in the citation is provided a composition or particularly a method to formulate the multiple units into a specific ready-to-use dosage form such as tablet, capsule etc.

It is known to a person skilled in art that multiple units such as pellets stated in the citation are essentially formulated as capsules, not compressed into tablets, primarily due to associated problems during compression of such multiple units such as rupture of units or the coating leading to a batch-to-batch variation in drug release. It is not obvious from the citation to one having ordinary skill in art to formulate controlled release layered tablet compositions of Nimesulide by seeing just the mere disclosure in the citation from such a large class of NSAIDs which have widely varying physicochemical properties such as solubility, flowability, particle size, pKa, permeability, therapeutic dose requirements, pharmacokinetics, etc.

PCT publication WO 99/12524 relates specifically to preparation of pellets (Refer particularly page 17, lines 33-34 of the cited reference and refer page 31, lines 31-35 of the cited reference). PCT publication WO 99/12524 further discloses that when appropriate, the first fraction is coated into homogeneous pellets (Refer page 17, lines 33-34 of the cited reference) and the second fraction comprises multiple units which are coated with a sustained release coating designed to release the drug substance in such a manner that the maintenance of a therapeutically active plasma concentration for a relatively long period of time are obtained (Refer page 1, lines 14-17 of the cited reference).

Furthermore, compositions and processes disclosed in the cited reference relate specifically to preparation of pellets as well as coating on pellets (Refer page 53, lines 11-12 of the cited reference) and preparation of granulates (Refer page 31,lines 2-4 of the cited reference and refer page 53, lines 10-11 of the cited reference). It is important to note that preparation and coating of pellets or granulates is a very cumbersome and cost intensive process. Further, a person skilled in art is neither taught nor motivated to form tablets from multiple units since it is disadvantageous to compress different fractions of multiple units, as the compression of such coated multiple units into tablets causes fracturing of particularly the coating layer, thereby causing

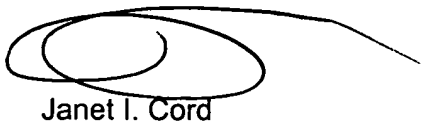
loss of reproducibility. Instead, the claimed invention specifically relates to tablet compositions comprising Nimesulide alongwith sustained release polymers, wherein the said polymers are used for coating the tablets which is the final dosage form thus preventing any fracture of coating or the dosage form, which in turn enhances batch-to-batch reproducibility and provides uniform drug release from the matrix tablet.

With regards to examiner's comments that it would have been obvious to one having ordinary skill in the art to have employed Nimesulide in the tablet/composition and one would have been motivated to do this in order to decrease the dosage amount of Nimesulide given to the patient, we beg to differ with the examiner's comments as the formulation of a tablet dosage form instead of multiple units does not lead to any change in the dosage amount of Nimesulide; instead the former being a single unit dosage form is easy to administer to a patient. Furthermore, PBL's invention has additional benefit with regards to patient compliance as the single unit tablet dosage form is a ready-to-use dosage form as compared to the multiple units disclosed in the cited reference since the multiple units such as pellets essentially have to be formulated into a single unit dosage form before administration.

Therefore, it is respectfully requested that this rejection be withdrawn.

Accordingly, applicants submit that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted



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